

Effect of PPAR δ Agonist on Stearoyl-CoA Desaturase 1 in Human Pancreatic Cancer Cells: Role of MEK/ERK1/2 Pathway

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Abstract

Objective

The stearoyl-CoA desaturase 1 (SCD1), also known as $\Delta 9$ -desaturase, is a regulatory enzyme in the cellular lipid modification process that has been linked to pancreatic cancer and diabetes. The aim of the present study was to investigate the effect of peroxisome proliferative-activated receptor δ (PPAR δ) agonist and ERK1/2- and EGF receptor (EGFR)-dependent pathways on the expression of SCD1 in human pancreatic carcinoma cell line PANC-1.

Methods

PANC-1 cells cultured in RPMI-1640 were exposed to the commonly used MEK inhibitor PD98059, EGFR-selective inhibitor AG1478, and PPAR δ agonist GW0742. Changes in mRNA, protein expression and activity index of SCD1 were then determined using real-time reverse transcription polymerase chain reaction, Western blot and gas liquid chromatography, respectively.

Results

The activity index and expression of SCD1 ($p < 0.01$) decreased following treatment with PPAR δ agonist at both mRNA and protein levels, whereas significant increases were observed after treatment with MEK or EGFR inhibitor. It was also found that the activity index of SCD1 were lower ($p < 0.01$) in the combined treatment compared to the incubation with either inhibitor alone.

Conclusions

PPAR δ and MEK/ERK1/2- and EGFR-dependent pathways affect the expression and activity of SCD1 in pancreatic cancer cells. Furthermore, the aforementioned kinase signalling pathways were involved in an inhibitory effect on the expression and activity of SCD1 in these cells, possibly via PPAR δ activation.